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(54) **CATIONIC OIL-IN-WATER EMULSIONS**

(75) Inventors: **Luis Brito**, Concord, MA (US);
Michelle Chan, Florence, MA (US);
Andrew Geall, Littleton, MA (US);
Derek O'Hagan, Winchester, MA (US);
Manmohan Singh, Cary, NC (US)

(73) Assignee: **GLAXOSMITHKLINE**
BIOLOGICALS SA (BE)

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See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

3,906,092 A 9/1975 Hilleman et al.
5,264,618 A 11/1993 Felgner et al.
5,384,133 A 1/1995 Boyes et al.
5,670,152 A 9/1997 Weiner et al.
5,712,257 A 1/1998 Carter
5,739,118 A 4/1998 Carrano et al.
5,795,587 A 8/1998 Gao et al.
5,906,980 A 5/1999 Carter
6,040,295 A 3/2000 Rolland et al.
6,086,901 A 7/2000 O'Hagan et al.
6,150,087 A 11/2000 Chien
6,171,586 B1 1/2001 Lam et al.
6,218,371 B1 4/2001 Krieger et al.
6,239,116 B1 5/2001 Krieger et al.
6,299,884 B1 10/2001 Van Nest et al.
6,306,405 B1 10/2001 O'Hagan et al.
6,451,325 B1 9/2002 Van Nest et al.
6,458,370 B1 10/2002 O'Hagan et al.
6,610,321 B2 8/2003 Huang et al.
6,855,492 B2 2/2005 O'Hagan et al.
6,861,410 B1 3/2005 Ott et al.
6,884,435 B1 4/2005 O'Hagan et al.
6,890,554 B2 5/2005 Jessee et al.
7,303,881 B2 12/2007 Huang et al.
7,314,627 B2 1/2008 Haynes et al.
7,550,145 B2 6/2009 O'Hagan et al.

(Continued)

FOREIGN PATENT DOCUMENTS

EP 00/50006 A2 8/2000
EP 1723972 A1 11/2006

(Continued)

OTHER PUBLICATIONS

Ott, G., et al., "A cationic sub-micron emulsion (MF59/DOTAP) is an effective delivery system for DNA vaccines", *J. Control Release*, 79(1-3): 1-5 (2002).
Yi, S.W., et al. "A cationic lipid emulsion/DNA complex as a physically stable and serum-resistant gene delivery system", *Pharm. Res.* 17(3): 314-320 (2000).
Kim, T.W., et al., "Optimization of Lipid Composition in Cationic Emulsion as In Vitro and In Vivo Transfection Agents", *Pharm. Res.* 18(1): 54-60 (2001).
Chung, H., et al. "Oil components modulate physical characteristics and function of the natural oil emulsions as drug or gene delivery system", *J. Control Release*, 71(3) 339-350 (2001).

(Continued)

Primary Examiner — Janet Epps-Smith
(74) *Attorney, Agent, or Firm* — Joseph J. Schuller;
Rebecca Stephens

(57) **ABSTRACT**

This invention generally relates to cationic oil-in-water emulsions that contain high concentrations of cationic lipids and have a defined oil:lipid ratio. The cationic lipid can interact with the negatively charged molecule thereby anchoring the molecule to the emulsion particles. The cationic emulsions described herein are useful for delivering negatively charged molecules, such as nucleic acid molecules to cells, and for formulating nucleic acid-based vaccines.